CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

75-456/458

CORRESPONDENCE

ABBOTT

Hospital Products Division
Abbott Laboratories
D-389, Bldg. AP30
200 Abbott Park Road
Abbott Park, Illinois 60064-6157

ORIG AMENDMENT
N/AM.

June 20, 2000

CENTER FOR DRUG EVALUATION AND RESEARCH
OFFICE OF GENERIC DRUGS, HFD # 630
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855

ATTENTION: Gary J. Buehler
Acting Director

RE: ANDA 75-456 Enalaprilat Injection, 1.25 mg/mL (Carpuject®)
ANDA 75-458 Enalaprilat Injection, 1.25 mg/mL (Vials)

MINOR AMENDMENT

Abbott Laboratories hereby amends the above-referenced abbreviated new drug applications for the subject drug products. This is in response to the Agency's tentative approval letter dated January 24, 2000.

Abbott Laboratories was informed in this letter that the reference listed drug (RLD) product, Vasotec I.V. Injection of Merck Research Laboratories, was awarded a six-month pediatric exclusivity for their U.S. Patent No. 4,374,829. We acknowledge that the above-referenced ANDAs were filed with a Paragraph III certification. The final approval of these drug products may not be made effective until the additional period of patent protection granted to the RLD holder expires on August 22, 2000.

We herein state that there have been no changes in the conditions under which the product was tentatively approved.

We look forward to receiving final approval for these ANDAs on August 22, 2000. Please contact me if you need any additional information.

Sincerely,

Abbott Laboratories

Jessie Y. Lee

Jessie Y. Lee, Ph.D.
Manager, Regulatory Affairs
Hospital Products Division
Phone: (847) 937-5513
Fax: (847) 938-7867
e-Mail: LEEJ@hpd.abbott.com

JYL:jl

G:\6-2000FDA.jyl/26

ABBOTT

Hospital Products Division
Abbott Laboratories
D-389, Bldg. AP30
200 Abbott Park Road
Abbott Park, Illinois 60064-6157

ORIG AMENDMENT

December 17, 1999

CENTER FOR DRUG EVALUATION AND RESEARCH
OFFICE OF GENERIC DRUGS, HFD # 630
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855

ATTENTION: Douglas Sporn
Director

RE: ANDA 75-456 Enalaprilat Injection, 1.25 mg/mL (Carpuject®)

MINOR AMENDMENT

Abbott Laboratories is pleased to respond to the Agency's letter of October 29, 1999, indicating tentative approval for the aforementioned ANDA. We acknowledge that this ANDA was filed with a Paragraph III certification and that final approval will not be made effective until U.S. Patent No. 4,374,829 expires on February 22, 2000.

We herein state that there have been no changes in the conditions under which the product was tentatively approved. Final printed labeling is supplied in Exhibit I of this submission.

We have also received tentative approval for our vial configuration, ANDA 75-458. Similar correspondence has been sent to that application.

We look forward to receiving final approval for this ANDA on February 22, 2000. Please contact me if you need any additional information.

Sincerely,

Abbott Laboratories

Jill Sackett
Associate Director, Regulatory Affairs
Hospital Products Division
Phone: (847) 937-4085
FAX: (847) 938-8967
12-99fda

ABBOTT

Hospital Products Division
Abbott Laboratories
D-389, Bldg. AP30
200 Abbott Park Road
Abbott Park, Illinois 60064-6157

August 6, 1999

CENTER FOR DRUG EVALUATION AND RESEARCH
OFFICE OF GENERIC DRUGS, HFD # 630
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855

NDA ORIG AMENDMENT
N/AM

ATTENTION: Douglas Sporn
Director

Re: ANDA 75-456 Enalaprilat Injection, 1.25 mg/mL (Carpuject®)

RESPONSE TO CHEMISTRY DEFICIENCIES

MINOR AMENDMENT

Abbott Laboratories hereby amends the above referenced abbreviated new drug application for the subject drug product submitted September 4, 1998 and amended May 7, 1999. We are responding to the Agency's action letter dated July 21, 1999. The Agency made the following comments:

A. Deficiencies

COMMENT: "1. **Please be advised that (has been reviewed and it remains deficient. The DMF holder has been advised of the deficiencies. Please do not respond to this letter until you have obtained a letter from the DMF holder stating that the DMF deficiencies have been satisfactorily resolved. A satisfactorily resolution of the DMF deficiencies is required prior to the approval of this ANDA."**

RESPONSE: We acknowledge that is currently deficicent and the DMF holder has been advised of the deficiencies. In addition, we acknowledge that a satisfactory resolution of the DMF deficiencies is required prior to the approval of this ANDA.

has advised us that they have satisfied all of the outstanding deficiencies in their or the bulk drug substance in their correspondence of July 29, 1999. Exhibit I contains a copy of the cover letter from

COMMENT: "2. **We note that you have revised your finished drug product degradation products release and stability specifications. Please provide revised finished drug product analytical methods reflecting these changes."**

CENTER FOR DRUG EVALUATION AND RESEARCH
RECD
AUG 09 1999
OGD

RESPONSE: Exhibit II contains the revised finished drug product test method for the degradation products to include the calculation of both known, unknown and total degradants/impurities.

B. In addition to responding to the deficiencies presented above, please note and acknowledge the following comments in your response:

COMMENT: **"1. Microbiological information you have provided is under review by our microbiologist. After the review is complete, any deficiencies found will be communicated to you under separate cover."**

RESPONSE: We note and acknowledge that our microbiological information is under review by FDA microbiologist and that any deficiencies found after the review is complete will be communicated to us under separate cover.

COMMENT: **"2. Since there is no official USP monograph for this finished drug product, the analytical methods will be validated in an FDA laboratory. The appropriate samples will be requested by the FDA at the appropriate time. However, please be advised that until you have addressed and resolved the deficiencies in this application, validation of your analytical methods by the FDA may be delayed."**

RESPONSE: We note and acknowledge that since there is no official USP monograph for this finished drug product the analytical methods will be validated in an FDA laboratory. We also note and acknowledge that the appropriate samples will be requested by the FDA at the appropriate time. In addition, please note that we have addressed all of the noted deficiencies in this correspondence.

COMMENT: **"3. We note that you have revised your finished drug product degradation products release and stability specifications. Please provide two additional separately bound copies of the analytical methods to reflect these changes. Test specifications and test data/COAs must be included in these analytical methods copies."**

RESPONSE: We have revised the finished drug product analytical method for the degradation products to include calculation for known, unknown and total degradants/impurities. Contained in Exhibit III are two additional separately bound copies of the finished drug product test method for the degradation products, including specifications and test data for the exhibit batches.

RESPONSE: Exhibit II contains the revised finished drug product test method for the degradation products to include the calculation of both known, unknown and total degradants/impurities.

C. **In addition to responding to the deficiencies presented above, please note and acknowledge the following comments in your response:**

COMMENT: "1. **Microbiological information you have provided is under review by our microbiologist. After the review is complete, any deficiencies found will be communicated to you under separate cover."**

RESPONSE: We note and acknowledge that our microbiological information is under review by FDA microbiologist and that any deficiencies found after the review is complete will be communicated to us under separate cover.

COMMENT: "2. **Since there is no official USP monograph for this finished drug product, the analytical methods will be validated in an FDA laboratory. The appropriate samples will be requested by the FDA at the appropriate time. However, please be advised that until you have addressed and resolved the deficiencies in this application, validation of your analytical methods by the FDA may be delayed."**

RESPONSE: We note and acknowledge that since there is no official USP monograph for this finished drug product the analytical methods will be validated in an FDA laboratory. We also note and acknowledge that the appropriate samples will be requested by the FDA at the appropriate time. In addition, please note that we have addressed all of the noted deficiencies in this correspondence.

COMMENT: "3. **We note that you have revised your finished drug product degradation products release and stability specifications. Please provide two additional separately bound copies of the analytical methods to reflect these changes. Test specifications and test data/COAs must be included in these analytical methods copies."**

RESPONSE: We have revised the finished drug product test method for the degradation products to include calculation for known, unknown and total degradants/impurities. Contained in Exhibit III are two additional separately bound copies of the revised finished drug product test method for the degradation products, including specifications and test data for the exhibit batches.

We trust that this submission is complete. If you require any clarification or further information, please telephone me at (847) 937-4085.

Sincerely,

Abbott Laboratories

Jill Sackett
Associate Director, Regulatory Affairs
Hospital Products Division
Phone: (847) 937-4085
FAX: (847) 938-8967
8-99fda

JUL 21 1999

38. CHEMISTRY COMMENTS TO BE PROVIDED TO THE APPLICANT

ANDA: **75-456** APPLICANT: **Abbott Laboratories**

DRUG PRODUCT: **Enalaprilat Injection, 1.25 mg/mL (Carpuject)**

The deficiencies presented below represent Minor deficiencies.

A. Deficiencies:

1. Please be advised that [redacted] has been reviewed and it remains deficient. The DMF holder has been advised of the deficiencies. Please do not respond to this letter until you have obtained a letter from the DMF holder stating that the DMF deficiencies have been satisfactorily resolved. A satisfactory resolution of the DMF deficiencies is required prior to the approval of this ANDA.

2. We note that you have revised your finished drug product degradation products release and stability specifications. Please provide revised finished drug product analytical methods reflecting these changes.

B. In addition to responding to the deficiencies presented above, please note and acknowledge the following comments in your response:

1. Microbiological information you have provided is under review by our microbiologist. After the review is complete, any deficiencies found will be communicated to you under separate cover.

2. Since there is no official USP monograph for this finished drug product, the analytical methods will be validated in an FDA laboratory. The appropriate samples will be requested by the FDA at the appropriate time. However, please be advised that until you have addressed and resolved the deficiencies in this application, validation of your analytical methods by the FDA may be delayed.

3. We note that you have revised your finished drug product degradation products release specifications. Please provide two additional separately bound copies of the analytical methods to reflect these changes. Test specifications and test data/COAs must be included in these analytical methods copies.

Sincerely yours,

Rashmikant M. Patel, Ph.D.
Director
Division of Chemistry I
Office of Generic Drugs
Center for Drug Evaluation and Research

ABBOTT

Hospital Products Division
Abbott Laboratories
D-389, Bldg. AP30
200 Abbott Park Road
Abbott Park, Illinois 60064-3537

May 7, 1999

ORIG AMENDMENT
N/A M

CENTER FOR DRUG EVALUATION AND RESEARCH
OFFICE OF GENERIC DRUGS, HFD # 630
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855

ATTENTION: Douglas Sporn
Director

ELECTRONIC SUBMISSION ENCLOSED

Re: ANDA 75-456 Enalaprilat Injection, 1.25 mg/mL (Carpuject®)

RESPONSE TO CHEMISTRY DEFICIENCIES

MINOR AMENDMENT

Abbott Laboratories hereby amends the above referenced abbreviated new drug application for the subject drug product submitted September 4, 1998. We are responding to the Agency's action letter dated April 19, 1999. The Agency made the following comments:

A. Deficiencies

COMMENT: "1.

RESPONSE:

COMMENT: "2.

RESPONSE:

MAY 10 19

GENERIC DRUGS

COMMENT: "3.

RESPONSE:

B. **In addition to responding to the deficiencies presented above, please note and acknowledge the following comments in your response:**

COMMENT: "1. **Please commit to update your raw material release specifications to reflect the most current USP supplements."**

RESPONSE: We confirm that the raw material ingredients (active and inactive) used in the manufacture of the drug product are compendial articles. Future testing will be in conformance with any future compendial revisions. In addition, please note that we have revised the specifications for Sodium Chloride and Water to reflect the most current USP supplements. Exhibit IV contains the revised specifications for Sodium Chloride and Water

Page(s) 1

Contain Trade Secret,

Commercial/Confidential

Information and are not

releasable.

5/7/99

RESPONSE: We note and acknowledge that the firms referenced in the application relative to the manufacture and testing of the product must be in compliance with cGMP(s) at the time of approval. FDA will request an evaluation from the Division of Manufacturing and Product Quality at the appropriate time.

COMMENT: "6. **Microbiological information you have provided is under review by our microbiologist. After the review is complete, any deficiencies found will be communicated to you under separate cover."**

RESPONSE: We note and acknowledge that our microbiological information is under review by FDA microbiologist and that any deficiencies found after the review is complete will be communicated to us under separate cover.

COMMENT: "7. **Since there is no official USP monograph for this finished drug product, the analytical methods will be validated in an FDA laboratory. The appropriate samples will be requested by the FDA at the appropriate time. However, please be advised that until you have addressed and resolved the deficiencies in this application, validation of your analytical methods by the FDA may be delayed."**

RESPONSE: We note and acknowledge that since there is no official USP monograph for this finished drug product the analytical methods will be validated in an FDA laboratory. We also note and acknowledge that the appropriate samples will be requested by the FDA at the appropriate time. In addition, please note that we have addressed all of the noted deficiencies in this correspondence.

We have also enclosed two diskettes (in duplicate and write protected) containing our electronic submission as part of the Office of Generic Drug (OGD's) electronic submission program using Entry Validation Application (EVA). A one page printout of the EVA log file is attached. The information included in the electronic submission is the same as the hardcopy paper submission.

We trust that this submission is complete. If you require any clarification or further information, please call me at (847) 937-4085.

Sincerely,

Abbott Laboratories

Jill Sackett
Associate Director, Regulatory Affairs
Hospital Products Division
Phone: (847) 937-4085
FAX: (847) 938-8967

ABBOTT

Hospital Products Division
Abbott Laboratories
D-389, Bldg. AP30
200 Abbott Park Road
Abbott Park, Illinois 60064-3537

May 31, 1999

NDA ORIG AMENDMENT

CENTER FOR DRUG EVALUATION AND RESEARCH
OFFICE OF GENERIC DRUGS, HFD # 630
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855

ATTENTION: Douglas Sporn
Director

ELECTRONIC SUBMISSION ENCLOSED

Re: ANDA 75-458 Enalaprilat Injection, 1.25 mg/mL (Vials)

RESPONSE TO CHEMISTRY AND LABELING DEFICIENCIES

MINOR AMENDMENT

Abbott Laboratories hereby amends the above referenced abbreviated new drug application for the subject drug product submitted September 4, 1998. We are responding to the Agency's action letter dated May 4, 1999. The Agency made the following comments:

A. Chemistry Deficiencies

COMMENT: "1.

RESPONSE:

ne

2-

COMMENT: "2.

e
is

RESPONSE:

RECD
JUN 14 1999
OGD
EVALUATION AND RESEARCH

COMMENT: "3. [illegible] Does this limit also apply to the unknown degradants? If [illegible]

RESPONSE: [illegible]

B. In addition to responding to the deficiencies presented above, please note and acknowledge the following comments in your response:

COMMENT: "1. **Please commit to update your raw material release specifications to reflect the most current USP supplements."**

RESPONSE: We confirm that the raw material ingredients (active and inactive) used in the manufacture of the drug product are compendial articles. Future testing will be in conformance with any future compendial revisions. In addition, please note that we have revised the specifications for Sodium Chloride and Water to reflect the most current USP supplements. Exhibit IV contains the revised specifications for Sodium Chloride and Water

Page(s) 1

Contain Trade Secret, Commercial/Confidential Information and are not releasable.

5/7/99

RESPONSE: We note and acknowledge that the firms referenced in the application relative to the manufacture and testing of the product must be in compliance with cGMP(s) at the time of approval. FDA will request an evaluation from the Division of Manufacturing and Product Quality at the appropriate time.

COMMENT: "6. **Microbiological information you have provided is under review by our microbiologist. After the review is complete, any deficiencies found will be communicated to you under separate cover."**

RESPONSE: We note and acknowledge that our microbiological information is under review by FDA microbiologist and that any deficiencies found after the review is complete will be communicated to us under separate cover.

COMMENT: "7. **Since there is no official USP monograph for this finished drug product, the analytical methods will be validated in an FDA laboratory. The appropriate samples will be requested by the FDA at the appropriate time. However, please be advised that until you have addressed and resolved the deficiencies in this application, validation of your analytical methods by the FDA may be delayed."**

RESPONSE: We note and acknowledge that since there is no official USP monograph for this finished drug product the analytical methods will be validated in an FDA laboratory. We also note and acknowledge that the appropriate samples will be requested by the FDA at the appropriate time. In addition, please note that we have addressed all of the noted deficiencies in this correspondence.

B. Labeling Deficiencies

We have revised our container labels and package insert as requested in the Agency's letter and supply revised final printed labeling in Exhibit VI. To facilitate review, we have provided a side-by-side comparison of our proposed labeling with our last submission with all differences annotated and explained.

We have also enclosed two diskettes (in duplicate and write protected) containing our electronic submission as part of the Office of Generic Drug (OGD's) electronic submission program using Entry Validation Application (EVA). A one page printout of the EVA log file is attached. The information included in the electronic submission is the same as the hardcopy paper submission.

We trust that this submission is complete. If you require any clarification or further information, please call me at (847) 937-4085.

Sincerely,

Abbott Laboratories

Jill Sackett
Associate Director, Regulatory Affairs
Hospital Products Division
Phone: (847) 937-4085
FAX: (847) 938-8967
5-99fda

APR 19 1999

38. CHEMISTRY COMMENTS TO BE PROVIDED TO THE APPLICANT

ANDA: **75-456** APPLICANT: **Abbott Laboratories/McPherson, KS2**

DRUG PRODUCT: **Enalaprilat Injection, 1.25 mg/mL (Carpuject)**

The deficiencies presented below represent minor deficiencies.

A. Deficiencies:

1. Please establish the limit of detection for the Enalaprilat drug substance related substance/impurities method.

2. Please be advised that) is currently deficient and the DMF holder has been advised of the deficiencies. A satisfactory resolution of the DMF deficiencies is required prior to the approval of this ANDA.

3. You have established a specification of or your finished drug product release and stability for individual degradation products. Does this limit also apply to the unknown degradants? If so, the limit % is not acceptable. Please revise and establish the limit based on the observed values.

B. In addition to responding to the deficiencies presented above, please note and acknowledge the following comments in your response:

1. Please commit to update your raw material release specifications to reflect the most current USP supplements.

2. Please explain the meaning of a "surrogate standard" as used in the validation of your Enalaprilat drug substance related substances

3. Please provide the definition and difference(s) for your Category I and II limit test classifications and the conditions under which these categories apply.

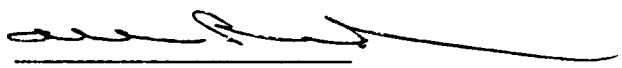
4. Please be advised that all DMF(s) referenced in this ANDA have to be found satisfactory at the time of approval of the ANDA. Some of the DMF holders may have to be inspected by our Division of Manufacturing and Product Quality. Any unsatisfactory review/evaluation will delay the approval of the ANDA.

5. The firms referenced in the application relative to the manufacture and testing of the product must be in compliance with cGMP(s) at the time of approval. We will request an evaluation from the Division of Manufacturing and Product Quality at the appropriate time.

6. Microbiological information you have provided is under review by our microbiologist. After the review is complete, any deficiencies found will be communicated to you under separate cover.

7. Since there is no official USP monograph for this finished drug product, the analytical methods will be validated in an FDA laboratory. The appropriate samples will be requested by the FDA at the appropriate time. However, please be advised that until you have addressed and resolved the deficiencies in this application, validation of your analytical methods by the FDA may be delayed.

Sincerely yours,



Rashmikant M. Patel, Ph.D.
Director
Division of Chemistry I
Office of Generic Drugs
Center for Drug Evaluation and Research

MAY - 4 1999

38. CHEMISTRY COMMENTS TO BE PROVIDED TO THE APPLICANT

AADA/ANDA: 75-458 APPLICANT: **Abbott Laboratories**

DRUG PRODUCT: **Enalaprilat Injection (Vials), 1.25 mg/mL**

The deficiencies presented below represent minor deficiencies.

A. Deficiencies:

1. Please establish the limit of detection for the Enalaprilat drug substance related substance/impurities method.

2. Please be advised that is currently deficient and the DMF holder has been advised of the deficiencies. A satisfactory resolution of the DMF deficiencies is required prior to the approval of this ANDA.

3. You have established a specification of for your finished drug product release and stability for individual degradation products. Does this limit also apply to the unknown degradants? If so, the limit s not acceptable. Please revise and establish the limit based on observed values.

B. In addition to responding to the deficiencies presented above, please note and acknowledge the following comments in your response:

1. Please commit to update your raw material release specifications to reflect the most current USP supplements.

2. Please explain the meaning of a "surrogate standard" as used in the validation of your Enalaprilat drug substance related substances method."

3. Please provide the definition and difference(s) for your Category I and II limit test classifications and the conditions under which these categories apply.

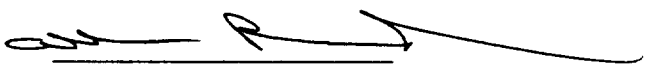
4. Please be advised that all DMF(s) referenced in this ANDA have to be found satisfactory at the time of approval of the ANDA. Some of the DMF holders may have to be inspected by our Division of Manufacturing and Product Quality. Any unsatisfactory review/evaluation will delay the approval of the ANDA.

5. The firms referenced in the application relative to the manufacture and testing of the product must be in compliance with cGMP(s) at the time of approval. We will request an evaluation from the Division of Manufacturing and Product Quality at the appropriate time.

6. Microbiological information you have provided is under review by our microbiologist. After the review is complete, any deficiencies found will be communicated to you under separate cover.

7. Since there is no official USP monograph for this finished drug product, the analytical methods will be validated in an FDA laboratory. The appropriate samples will be requested by the FDA at the appropriate time. However, please be advised that until you have addressed and resolved the deficiencies in this application, validation of your analytical methods by the FDA may be delayed.

Sincerely yours,



Rashmikant M. Patel, Ph.D.
Director
Division of Chemistry I
Office of Generic Drugs
Center for Drug Evaluation and Research

BIOEQUIVALENCY COMMENTS TO BE PROVIDED TO THE APPLICANT

ANDA: 75456 APPLICANT: Abbott Laboratories

DRUG PRODUCT: Enalaprilat Injection (1.25 mg/ml)

The Division of Bioequivalence has completed its review and has no further questions at this time.

Please note that the bioequivalency comments provided in this communication are preliminary. These comments are subject to revision after review of the entire application, upon consideration of the chemistry, manufacturing and controls, microbiology, labeling, or other scientific or regulatory issues. Please be advised that these reviews may result in the need for additional bioequivalency information and/or studies, or may result in a conclusion that the proposed formulation is not approvable.

Sincerely yours,

Dale P. Conner, Pharm. D.
Director
Division of Bioequivalence
Office of Generic Drugs
Center for Drug Evaluation and Research

ABBOTT

Hospital Products Division
Abbott Laboratories
D-389, Bldg. AP30
200 Abbott Park Road
Abbott Park, Illinois 60064-3537

ORIG AMENDMENT
N/AC

November 23, 1998

CENTER FOR DRUG EVALUATION AND RESEARCH
OFFICE OF GENERIC DRUGS, HFD #630
Metro Park North II
7500 Standish Place, Room 150
Rockville, Maryland 20855

ATTENTION: Douglas Sporn
Director

RE: 75-456 Enalaprilat Injection 1.25mg/mL, (Carpuject)

AMENDMENT

Abbott Laboratories hereby amends the above referenced original abbreviated new drug application for the subject drug submitted September 4, 1998. We are responding to the phone call November 5, 1998 from the Agency to Nancy Conway, Abbott Laboratories. Reference is made to the amendment dated October 28, 1998.

The Agency's requests are as follows:

"We are refusing to file this ANDA under 21 CFR 314.101 (d)(2) for the following reasons:"

REQUEST: **1. The application lacks side by side comparisons of the proposed labeling versus the labeling for the reference listed drug with all of the differences annotated and explained. The side by side labeling submitted in the amendment dated October 28, 1998 is not adequate.**

RESPONSE: Provided in EXHIBIT I is the side by side labeling as requested by the Agency.

REQUEST: **2. Please provide signed certification that the third (field) copy of the application has been submitted to the appropriate district office and a statement that it is a "true copy" of the technical sections contained in the application. Also, provide original copies of the "List of Relevant Convictions for Persons Debarred or Not Debarred", "Certification Requirement for all Applications for Approval of a Drug Product Concerning Using Services of Debarred Persons" and "Patent Certification and Exclusivity Statement."**

RESPONSE: The requested information was previously included in the original ANDA dated September 4, 1998. These documents are located on pages as listed below. However for the convenience of the Agency, we provide new original documents with signatures dated today in EXHIBIT II.

1. CERTIFICATION THAT THE THIRD (FIELD) COPY OF THE APPLICATION HAS BEEN SUBMITTED TO THE APPROPRIATE DISTRICT OFFICE AND A STATEMENT THAT IT IS A "TRUE COPY" OF THE TECHNICAL SECTIONS CONTAINED IN THE APPLICATION. (Vol. 1, pg 2 of cover letter)

2. LIST OF RELEVANT CONVICTIONS FOR PERSONS DEBARRED OR NOT DEBARRED (Vol. 1, pg 3)

3. CERTIFICATION REQUIREMENT FOR ALL APPLICATIONS FOR APPROVAL OF A DRUG PRODUCT CONCERNING USING SERVICES OF DEBARRED PERSONS (Vol. 1, pg 4)

4. PATENT CERTIFICATION AND EXCLUSIVITY STATEMENT (Vol. 1, pg 8)

If you require any further clarification or further information, please call me at 847-937-3413.

Sincerely,

Jean Conaway, R.Ph.
Manager, Regulatory Affairs
Hospital Products Division
Phone: (847) 937-3413
Fax: (847) 938-7867

JMC:jmc

G:\11-98fda.jmc23

BIOEQUIVALENCY COMMENTS TO BE PROVIDED TO THE APPLICANT

ANDA: 75458 APPLICANT: Abbott Laboratories

DRUG PRODUCT: Enalaprilat Injection (1.25 mg/mL)

The Division of Bioequivalence has completed its review and has no further questions at this time.

Please note that the bioequivalency comments provided in this communication are preliminary. These comments are subject to revision after review of the entire application, upon consideration of the chemistry, manufacturing and controls, microbiology, labeling, or other scientific or regulatory issues. Please be advised that these reviews may result in the need for additional bioequivalency information and/or studies, or may result in a conclusion that the proposed formulation is not approvable.

Sincerely yours,

Dale P. Conner

Dale P. Conner, Pharm. D.
Director
Division of Bioequivalence
Office of Generic Drugs
Center for Drug Evaluation and Research

BIOEQUIVALENCY COMMENTS TO BE PROVIDED TO THE APPLICANT

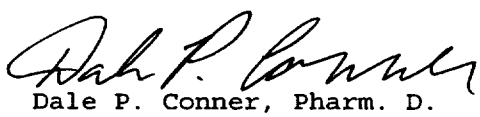
ANDA: 75458 APPLICANT: Abbott Laboratories

DRUG PRODUCT: Enalaprilat Injection (1.25 mg/mL)

The Division of Bioequivalence has completed its review and has no further questions at this time.

Please note that the bioequivalency comments provided in this communication are preliminary. These comments are subject to revision after review of the entire application, upon consideration of the chemistry, manufacturing and controls, microbiology, labeling, or other scientific or regulatory issues. Please be advised that these reviews may result in the need for additional bioequivalency information and/or studies, or may result in a conclusion that the proposed formulation is not approvable.

Sincerely yours,



Dale P. Conner, Pharm. D.
Director
Division of Bioequivalence
Office of Generic Drugs
Center for Drug Evaluation and Research

BIOEQUIVALENCY COMMENTS TO BE PROVIDED TO THE APPLICANT

ANDA: 75456 APPLICANT: Abbott Laboratories

DRUG PRODUCT: Enalaprilat Injection (1.25 mg/ml)

The Division of Bioequivalence has completed its review and has no further questions at this time.

Please note that the bioequivalency comments provided in this communication are preliminary. These comments are subject to revision after review of the entire application, upon consideration of the chemistry, manufacturing and controls, microbiology, labeling, or other scientific or regulatory issues. Please be advised that these reviews may result in the need for additional bioequivalency information and/or studies, or may result in a conclusion that the proposed formulation is not approvable.

Sincerely yours,

Dale P. Conner, Pharm. D.
Director
Division of Bioequivalence
Office of Generic Drugs
Center for Drug Evaluation and Research

ANDA 75-456

Abbott Laboratories
Attention: Jean Conaway
200 Abbott Park Road D-389/AP30
Abbott Park, IL 60064-3500

NOV 20 1998

Dear Madam:

We acknowledge the receipt of your abbreviated new drug application submitted pursuant to Section 505(j) of the Federal Food, Drug and Cosmetic Act.

Reference is also made to your amendment dated October 28, 1998.

NAME OF DRUG: Enalaprilat Injection 1.25 mg/mL (syringe)

DATE OF APPLICATION: September 4, 1998

DATE (RECEIVED) ACCEPTABLE FOR FILING: October 30, 1998

We will correspond with you further after we have had the opportunity to review your application.

In the interim, please provide **side-by-side** comparisons of the proposed labeling versus the labeling for the reference listed drug with all of the **differences annotated and explained.** Labeling is defined in the regulations to include both container labels and package insert labeling. Please provide this comparison with all differences annotated and explained as per 21 CFR 314.94(a)(8)(iv).

Please identify any communications concerning this application with the number shown above.

Should you have questions concerning this application contact:

Pat Beers-Block
Project Manager
(301) 827-5848

Sincerely yours,

Jerry Phillips
Director,
Division of Labeling and Program Support
Office of Generic Drugs
Center for Drug Evaluation and Research

ANDA
CC:

date 11/30/98
date 11/10/98

ABBOTT

NDA ORIG AMENDMENT
AC

Hospital Products Division
Abbott Laboratories
D-389, Bldg. AP30
200 Abbott Park Road
Abbott Park, Illinois 60064-3537

October 28, 1998

CENTER FOR DRUG EVALUATION AND RESEARCH
OFFICE OF GENERIC DRUGS, HFD #630
Metro Park North II
7500 Standish Place, Room 150
Rockville, Maryland 20855

ATTENTION: Douglas Spom
Director

Re: 75-456 Enalaprilat Injection 1.25mg/mL, (Carpuject)

AMENDMENT

Abbott Laboratories hereby amends the above-referenced original abbreviated new drug application for the subject drug submitted September 4, 1998. We are responding to the letter dated October 13, 1998 from the Agency.

The Agency's requests are as follows:

"We are refusing to file this ANDA under 21 CFR 314.101 (d)(2) for the following reasons:"

REQUEST: **1. "The application lacks side-by-side comparisons of the proposed labeling versus the labeling for the reference listed drug with all of the differences annotated and explained. Labeling is defined in the regulations to include both container labels and package insert labeling. Please provide this comparison with all differences annotated and explained as per 21 CFR 314.94 (a) (8) (iv)."**

RESPONSE: A copy of the side-by-side labeling is found in the original submission on pages 1-20A through 1-20W. For convenience of the Agency another copy is provided in EXHIBIT I.

REQUEST: **2. "You have failed to provide a signed certification that the third (field) copy of the application has been submitted to the appropriate district office and a statement that it is a "true copy" of the technical sections contained in the application."**

RESPONSE: Provided in EXHIBIT II is a copy of the cover letter that was included in the original submission. This cover letter includes the certification that the third (field copy) of the application has been submitted to the appropriate district office. The certification included within the cover letter is as follows:

"Abbott Laboratories hereby certify that we have sent a true copy of this submission to Mr. W. Michael Rogers of the Lenexa, Kansas FDA District Office."

REQUEST: 3. "The strength on the 356h form should be changed from 1.25 mL to 1.25 mg/mL."

RESPONSE: The above request has been acknowledged and the FDA FORM 356h has been revised and included in EXHIBIT III. We regret any inconvenience that this typographical error may have caused the Agency.

REQUEST: 4. "Please provide a readable copy of the Nitrogen Certificate of Analysis (COA) on page 2-56."

RESPONSE: Provided in EXHIBIT IV is a readable revised copy the Nitrogen Certificate of Analysis (COA).

We trust that this submission is complete and can be expeditiously approved. Please telephone me at your earliest convenience if I can provide additional information.

Sincerely,

Jean Conaway, R.Ph.
Manager, Regulatory Affairs
Hospital Products Division
Phone: (847) 937-3413
Fax: (847) 938-7867

JMC:jmc

G:\10-98fda.jmc40

ABBOTT

Hospital Products Division
Abbott Laboratories
D-389, Bldg. AP30
200 Abbott Park Road
Abbott Park, Illinois 60064-3537

ORIG AMENDMENT
N/AC

November 23, 1998

CENTER FOR DRUG EVALUATION AND RESEARCH
OFFICE OF GENERIC DRUGS, HFD #630
Metro Park North II
7500 Standish Place, Room 150
Rockville, Maryland 20855

ATTENTION: Douglas Sporn
Director

RE: 75-458 Enalaprilat Injection 1.25mg/mL, (Vial)

AMENDMENT

Abbott Laboratories hereby amends the above referenced original abbreviated new drug application for the subject drug submitted September 4, 1998. We are responding to the phone call November 5, 1998 from the Agency to Nancy Conway, Abbott Laboratories. Reference is made to the amendment dated October 28, 1998.

The Agency's requests are as follows:

"We are refusing to file this ANDA under 21 CFR 314.101 (d)(2) for the following reasons:"

REQUEST: **1. The application lacks side by side comparisons of the proposed labeling versus the labeling for the reference listed drug with all of the differences annotated and explained. The side by side labeling submitted in the amendment dated October 28, 1998 is not adequate.**

RESPONSE: Provided in EXHIBIT I is the side by side labeling as requested by the Agency.

REQUEST: **2. Please provide signed certification that the third (field) copy of the application has been submitted to the appropriate district office and a statement that it is a "true copy" of the technical sections contained in the application. Also, provide original copies of the "List of Relevant Convictions for Persons Debarred or Not Debarred", "Certification Requirement for all Applications for Approval of a Drug Product Concerning Using Services of Debarred Persons" and "Patent Certification and Exclusivity Statement".**

RECEIVED
NOV 30 1998
GENERIC DRUGS

RESPONSE: The requested information was previously included in the original ANDA dated September 4, 1998. These documents are located on pages as listed below. However for the convenience of the Agency, we provide new original documents with signatures dated today in EXHIBIT II.

1. CERTIFICATION THAT THE THIRD (FIELD) COPY OF THE APPLICATION HAS BEEN SUBMITTED TO THE APPROPRIATE DISTRICT OFFICE AND A STATEMENT THAT IT IS A "TRUE COPY" OF THE TECHNICAL SECTIONS CONTAINED IN THE APPLICATION. **(Vol. 1, pg 2 of cover letter)**
2. LIST OF RELEVANT CONVICTIONS FOR PERSONS DEBARRED OR NOT DEBARRED **(Vol. 1, pg 3)**
3. CERTIFICATION REQUIREMENT FOR ALL APPLICATIONS FOR APPROVAL OF A DRUG PRODUCT CONCERNING USING SERVICES OF DEBARRED PERSONS **(Vol. 1, pg 4)**
4. PATENT CERTIFICATION AND EXCLUSIVITY STATEMENT **(Vol. 1, pg 8)**

If you require any further clarification or further information, please call me at 847-937-3413.

Sincerely,

Jean Conaway, R.Ph.
Manager, Regulatory Affairs
Hospital Products Division
Phone: (847) 937-3413
Fax: (847) 938-7867

JMC:jmc

G:\11-98fda.jmc27

ANDA 75-458

Abbott Laboratories
Attention: Jean Conaway
200 Abbott Park Road D-389/AP30
Abbott Park, IL 60064-3500

NOV 20 1998

Dear Madam:

We acknowledge the receipt of your abbreviated new drug application submitted pursuant to Section 505(j) of the Federal Food, Drug and Cosmetic Act.

Reference is also made to your amendment dated October 28, 1998.

NAME OF DRUG: Enalaprilat Injection, 1.25 mg/mL (vial)

DATE OF APPLICATION: September 4, 1998

DATE (RECEIVED) ACCEPTABLE FOR FILING: October 30, 1998

We will correspond with you further after we have had the opportunity to review your application.

In the interim, please provide **side-by-side** comparisons of the proposed labeling versus the labeling for the reference listed drug with all of the **differences annotated and explained.** Labeling is defined in the regulations to include both container labels and package insert labeling. Please provide this comparison with all differences annotated and explained as per 21 CFR 314.94(a)(8)(iv).

Please identify any communications concerning this application with the number shown above.

Should you have questions concerning this application contact:

Pat Beers-Block
Project Manager
(301) 827-5848

Sincerely yours,

Jerry Phillips
Director,
Division of Labeling and Program Support
Office of Generic Drugs
Center for Drug Evaluation and Research

ANDA 75-458
cc:

HFD-615/MBennett

date 11/20/98
date 11/10/98
date

K

ANDA 75-456

Abbott Laboratories
Attention: Jean Conaway
200 Abbott Park Road D-389/AP30
Abbott Park, IL 60064-3500

OCT 13 1998

Dear Madam:

Please refer to your abbreviated new drug application (ANDA) dated September 4, 1998, submitted under Section 505(j) of the Federal Food, Drug and Cosmetic Act for Enalaprilat Injection 1.25 mg/mL (syringe).

We have given your application a preliminary review, and we find that it is not sufficiently complete to merit a critical technical review.

We are refusing to file this ANDA under 21 CFR 314.101(d)(2) for the following reasons:

The application lacks side-by-side comparisons of the proposed labeling versus the labeling for the reference listed drug with all of the differences annotated and explained. Labeling is defined in the regulations to include both container labels and package insert labeling. Please provide this comparison with all differences annotated and explained as per 21 CFR 314.94(a)(8)(iv).

You have failed to provide a signed certification that the third (field copy) of the application has been submitted to the appropriate district office and a statement that it is a "true copy" of the technical sections contained in the application.

Thus, it will not be filed as an abbreviated new drug application within the meaning of Section 505(j) of the Act.

The strength on the 356h form should be changed from 1.25 mL to 1.25 mg/mL.

Please provide a readable copy of the Nitrogen Certificate of Analysis (COA) on page 2-56.

Within 30 days of the date of this letter you may amend your application to include the above information or request in

writing an informal conference about our refusal to file the application. To file this application over FDA's protest, you must avail yourself of this informal conference.

If after the informal conference, you still do not agree with our conclusion, you may make a written request to file the application over protest, as authorized by 21 CFR 314.101(a)(3). If you do so, the application shall be filed over protest under 21 CFR 314.101(a)(2). The filing date will be 60 days after the date you requested the informal conference. If you have any questions please call:

Saundra T. Middleton
Project Manager
(301) 827-5862

Sincerely yours,

Jerry Phillips
Director
Division of Labeling and Program Support
Office of Generic Drugs
Center for Drug Evaluation and Research

ANDA
cc:

[illegible]/Phillips

0/13/98
ate 10/13/9

ANDA Refuse to File:

ABBOTT

Hospital Products Division
Abbott Laboratories
D-389, Bldg. AP30
200 Abbott Park Road
Abbott Park, Illinois 60064-3537

September 4, 1998

CENTER FOR DRUG EVALUATION AND RESEARCH
OFFICE OF GENERIC DRUGS, HFD # 630
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855

ATTENTION: Douglas Sporn
Director

ELECTRONIC SUBMISSION ENCLOSED

Re: Enalaprilat Injection, 1.25 mg/mL (Carpuject®)
Original Abbreviated New Drug Application

Dear Mr. Sporn:

Abbott Laboratories hereby submits an abbreviated new drug application for Enalaprilat Injection, 1.25 mg/mL, 1 mL fill in 2 mL Carpuject® in accordance with Section 505(j) of the Federal Food Drug and Cosmetic Act. The subject drug is a prescription drug and not an over-the-counter drug. In June, 1997, Abbott Laboratories purchased the Sanofi Winthrop Pharmaceuticals manufacturing facility in McPherson, Kansas. This original ANDA applies to that manufacturing facility. The establishment registration number of the McPherson, Kansas facility is 1925262.

Enalaprilat Injection is listed in "Approved Drug Products with Therapeutic Equivalence Evaluations," 17th Edition, page 3-123. A copy appears in Section II.

The active ingredient, indications (applicable to the injection), route of administration, dosage form, and strength for Enalaprilat Injection are the same as those of the innovator's product, Vasotec® I.V., sponsored by Merck & Co., Inc. Comparative information is contained in Section IV.

The labeling is the same in content as that of the reference drug, Vasotec® I.V., except for changes that are necessary due to a change in manufacturer. A copy of the innovator's package insert is provided in Section V.

The first three production batches of Enalaprilat Injection, 1.25 mg/mL, 1 mL fill in 2 mL Carpuject®, will be placed into our stability program and reported at regular intervals for as long as necessary to support the proposed 24-month expiration date. Furthermore, we agree to withdraw from the market any batch found to fall outside the established specifications for this product. Our complete stability protocol and post-approval commitments are contained in Section XVII.

For the convenience of the Agency, documentation for Sterilization Process Validation is contained in a separate volume with a dedicated table of contents.

We have also enclosed two diskettes (in duplicate and write protected) containing our electronic submission as part of the Office of Generic Drugs (OGD's) electronic submission program using Entry Validation Application (EVA). A one page printout of the EVA log file is attached. The information included in the electronic submission is the same as the hardcopy paper submission.

Abbott Laboratories hereby certify that we have sent a true copy of this submission to Mr. W. Michael Rogers of the Lenexa, Kansas FDA District Office.

This document consists of Confidential and/or Trade Secret information subject to 18 U.S.C. 1905 and to which all claims of Privilege and Confidentiality are asserted in both statutory and common law.

If you require any clarification or further information, please call me at (847) 937-3413.

Sincerely,

ABBOTT LABORATORIES

Jean Conaway
Manager, Regulatory Affairs
Hospital Products Division
Phone: (847) 937-3413
FAX: (847) 937-7867

G: 9-98fda.jmc.doc

ABBOTT

Hospital Products Division
Abbott Laboratories
D-389, Bldg. AP30
200 Abbott Park Road
Abbott Park, Illinois 60064-3537

October 28, 1998

CENTER FOR DRUG EVALUATION AND RESEARCH
OFFICE OF GENERIC DRUGS, HFD #630
Metro Park North II
7500 Standish Place, Room 150
Rockville, Maryland 20855

NDA ORIG AMENDMENT
AC

ATTENTION: Douglas Sporn
Director

Re: 75-458 Enalaprilat Injection 1.25mg/mL (Vial)

AMENDMENT

Abbott Laboratories hereby amends the above-referenced original abbreviated new drug application for the subject drug submitted September 4, 1998. We are responding to the letter dated October 13, 1998 from the Agency.

The Agency's requests are as follows:

"We are refusing to file this ANDA under 21 CFR 314.101 (d)(2) for the following reasons:"

REQUEST: **1. "The application lacks side-by-side comparisons of the proposed labeling versus the labeling for the reference listed drug with all of the differences annotated and explained. Labeling is defined in the regulations to include both container labels and package insert labeling. Please provide this comparison with all differences annotated and explained as per 21 CFR 314.94 (a) (8) (iv)."**

RESPONSE: A copy of the side-by-side labeling is found in the original submission on pages 1-21A through 1-21R. For convenience of the Agency another copy is provided in EXHIBIT I.

REQUEST: **2. "The strength on the 356h form should be changed from 1.25 mL to 1.25 mg/mL."**

RESPONSE: The above request has been acknowledged and the FDA FORM 356h has been revised and included in EXHIBIT II. We regret any inconvenience that this typographical error may have caused the Agency.

RECEIVED
OCT 30 1998

REQUEST: **3. "Please provide a readable copy of the Nitrogen Certificate of Analysis (COA) on page 2-56."**

RESPONSE: Provided in EXHIBIT III is a readable revised copy the Nitrogen Certificate of Analysis (COA).

We trust that this submission is complete and can be expeditiously approved. Please telephone me at your earliest convenience if I can provide additional information.

Sincerely,

Jean Conaway, R.Ph.
Manager, Regulatory Affairs
Hospital Products Division
Phone: (847) 937-3413
Fax: (847) 938-7867

JMC:jmc

G:\10-98fda.jmc35

ANDA 75-458

Abbott Laboratories Conaway
Attention: Jean ~~Conway~~
200 Abbott Park Road D-389/AP30
Abbott Park, IL 60064-3500

OCT 13 1998

Dear Madam:

Please refer to your abbreviated new drug application (ANDA) dated September 4, 1998, submitted under Section 505(j) of the Federal Food, Drug and Cosmetic Act for Enalaprilat Injection, 1.25 mg/mL (vial).

We have given your application a preliminary review, and we find that it is not sufficiently complete to merit a critical technical review.

We are refusing to file this ANDA under 21 CFR 314.101(d)(2) for the following reasons:

The application lacks side-by-side comparisons of the proposed labeling versus the labeling for the reference listed drug with all of the differences annotated and explained. Labeling is defined in the regulations to include both container labels and package insert labeling. Please provide this comparison with all differences annotated and explained as per 21 CFR 314.94(a)(8)(iv).

Thus, it will not be filed as an abbreviated new drug application within the meaning of Section 505(j) of the Act.

The strength on the 356h form should be changed from 1.25 mL to 1.25 mg/mL.

Please provide a readable copy of the Nitrogen Certificate of Analysis (COA) on page 2-56.

Within 30 days of the date of this letter you may amend your application to include the above information or request in writing an informal conference about our refusal to file the

application. To file this application over FDA's protest, you must avail yourself of this informal conference.

If after the informal conference, you still do not agree with our conclusion, you may make a written request to file the application over protest, as authorized by 21 CFR 314.101(a)(3). If you do so, the application shall be filed over protest under 21 CFR 314.101(a)(2). The filing date will be 60 days after the date you requested the informal conference. If you have any questions please call:

Saundra T. Middleton
Project Manager
(301) 827-5862

Sincerely yours,

Jerry Phillips
Director
Division of Labeling and Program Support
Office of Generic Drugs
Center for Drug Evaluation and Research

ANDA 75-458
cc:

E

ABBOTT

NEW DRUG APPLICATION

Hospital Products Division
Abbott Laboratories
D-389, Bldg. AP30
200 Abbott Park Road
Abbott Park, Illinois 60064-3537

September 4, 1998

CENTER FOR DRUG EVALUATION AND RESEARCH
OFFICE OF GENERIC DRUGS, HFD # 630
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855

ATTENTION: Douglas Sporn
Director

ELECTRONIC SUBMISSION ENCLOSED

Re: Enalaprilat Injection, 1.25 mg/mL (Vial)
Original Abbreviated New Drug Application

Dear Mr. Sporn:

Abbott Laboratories hereby submits an abbreviated new drug application for Enalaprilat Injection, 1.25 mg/mL, 1 mL fill in 2 mL vial and 2 mL fill in 2 mL vial in accordance with Section 505(j) of the Federal Food Drug and Cosmetic Act. The subject drug is a prescription drug and not an over-the-counter drug. In June, 1997, Abbott Laboratories purchased the Sanofi Winthrop Pharmaceuticals manufacturing facility in McPherson, Kansas. This original ANDA applies to that manufacturing facility. The establishment registration number of the McPherson, Kansas facility is 1925262.

Enalaprilat Injection is listed in "Approved Drug Products with Therapeutic Equivalence Evaluations," 17th Edition, page 3-123. A copy appears in Section II.

The active ingredient, indications (applicable to the injection), route of administration, dosage form, and strength for Enalaprilat Injection are the same as those of the innovator's product, Vasotec® I.V., sponsored by Merck & Co., Inc. Comparative information is contained in Section IV.

The labeling is the same in content as that of the reference drug, Vasotec® I.V., except for changes that are necessary due to a change in manufacturer. A copy of the innovator's package insert is provided in Section V.

The first three production batches of Enalaprilat Injection, 1.25 mg/mL, 1 mL fill in 2 mL vial and 2 mL fill in 2 mL vial, will be placed into our stability program and reported at regular intervals for as long as necessary to support the proposed 24-month expiration date. Furthermore, we agree to withdraw from the market any batch found to fall outside the established specifications for this product. Our complete stability protocol and post-approval commitments are contained in Section XVII.

For the convenience of the Agency, documentation for Sterilization Process Validation is contained in a separate volume with a dedicated table of contents.

We have also enclosed two diskettes (in duplicate and write protected) containing our electronic submission as part of the Office of Generic Drugs (OGD's) electronic submission program using Entry Validation Application (EVA). A one page printout of the EVA log file is attached. The information included in the electronic submission is the same as the hardcopy paper submission.

Abbott Laboratories hereby certify that we have sent a true copy of this submission to Mr. W. Michael Rogers of the Lenexa, Kansas FDA District Office.

This document consists of Confidential and/or Trade Secret information subject to 18 U.S.C. 1905 and to which all claims of Privilege and Confidentiality are asserted in both statutory and common law.

If you require any clarification or further information, please call me at (847) 937-3413.

Sincerely,

ABBOTT LABORATORIES

Jean Conaway

Jean Conaway
Manager, Regulatory Affairs
Hospital Products Division
Phone: (847) 937-3413
FAX: (847) 937-7867

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ABBOTT

Hospital Products Division
Abbott Laboratories
D-389, Bldg. AP30
200 Abbott Park Road
Abbott Park, Illinois 60064-6157

December 17, 1999

ORIG AMENDMENT
N/AM

CENTER FOR DRUG EVALUATION AND RESEARCH
OFFICE OF GENERIC DRUGS, HFD # 630
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855

ATTENTION: Douglas Sporn
Director

ANDA 75-458 Enalaprilat Injection, 1.25 mg/mL (Vials)

MINOR AMENDMENT

Abbott Laboratories is pleased to respond to the Agency's letter of October 29, 1999, indicating tentative approval for the aforementioned ANDA. We acknowledge that this ANDA was filed with a Paragraph III certification and that final approval will not be made effective until U.S. Patent No. 4,374,829 expires on February 22, 2000.

We herein state that there have been no changes in the conditions under which the product was tentatively approved. Final printed labeling is supplied in Exhibit I of this submission.

We have also received tentative approval for our Carpuject® configuration, ANDA 75-456. Similar correspondence has been sent to that application.

We look forward to receiving final approval for this ANDA on February 22, 2000. Please contact me if you need any additional information.

Sincerely,

Abbott Laboratories

JSackett

Jill Sackett
Associate Director, Regulatory Affairs
Hospital Products Division
Phone: (847) 937-4085
FAX: (847) 938-8967
12-99fda

We trust that this submission is complete. If you require any clarification or further information, please telephone me at (847) 937-4085.

Sincerely,

Abbott Laboratories

Jill Sackett
Associate Director, Regulatory Affairs
Hospital Products Division
Phone: (847) 937-4085
FAX: (847) 938-8967
8-99fda

ABBOTT

Hospital Products Division
Abbott Laboratories
D-389, Bldg. AP30
200 Abbott Park Road
Abbott Park, Illinois 60064-6157

ORIG AMENDMENT
N/AM.

June 20, 2000

CENTER FOR DRUG EVALUATION AND RESEARCH
OFFICE OF GENERIC DRUGS, HFD # 630
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855

ATTENTION: Gary J. Buehler
Acting Director

RE: ANDA 75-456 Enalaprilat Injection, 1.25 mg/mL (Carpuject®)
ANDA 75-458 Enalaprilat Injection, 1.25 mg/mL (Vials)

MINOR AMENDMENT

Abbott Laboratories hereby amends the above-referenced abbreviated new drug applications for the subject drug products. This is in response to the Agency's tentative approval letter dated January 24, 2000.

Abbott Laboratories was informed in this letter that the reference listed drug (RLD) product, Vasotec I.V. Injection of Merck Research Laboratories, was awarded a six-month pediatric exclusivity for their U.S. Patent No. 4,374,829. We acknowledge that the above-referenced ANDAs were filed with a Paragraph III certification. The final approval of these drug products may not be made effective until the additional period of patent protection granted to the RLD holder expires on August 22, 2000.

We herein state that there have been no changes in the conditions under which the product was tentatively approved.

We look forward to receiving final approval for these ANDAs on August 22, 2000. Please contact me if you need any additional information.

Sincerely,

Abbott Laboratories

Jessie Y. Lee

Jessie Y. Lee, Ph.D.
Manager, Regulatory Affairs
Hospital Products Division
Phone: (847) 937-5513
Fax: (847) 938-7867
e-Mail: LEEJ@hpd.abbott.com

JYL:jl

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JUL 21 1999

38. CHEMISTRY COMMENTS TO BE PROVIDED TO THE APPLICANT

ANDA: **75-458** APPLICANT: **Abbott Laboratories**

DRUG PRODUCT: **Enalaprilat Injection (Vials), 1.25 mg/mL**

The deficiencies presented below represent Minor deficiencies.

A. Deficiencies:

1. Please be advised that has been reviewed and it remains deficient. The DMF holder has been advised of the deficiencies. Please do not respond to this letter until you have obtained a letter from the DMF holder stating that the DMF deficiencies have been satisfactorily resolved. A satisfactory resolution of the DMF deficiencies is required prior to the approval of this ANDA.

2. We note that you have revised your finished drug product degradation products release and stability specifications. Please provide revised finished drug product analytical methods reflecting these changes.

B. In addition to responding to the deficiencies presented above, please note and acknowledge the following comments in your response:

1. Microbiological information you have provided is under review by our microbiologist. After the review is complete, any deficiencies found will be communicated to you under separate cover.

2. Since there is no official USP monograph for this finished drug product, the analytical methods will be validated in an FDA laboratory. The appropriate samples will be requested by the FDA at the appropriate time. However, please be advised that until you have addressed and resolved the deficiencies in this application, validation of your analytical methods by the FDA may be delayed.

3. We note that you have revised your finished drug product degradation products release specifications. Please provide two additional separately bound copies of the analytical methods to reflect these changes. Test specifications and test data /COAs must be included in these analytical methods copies.

Sincerely yours,

Rashmikant M. Patel, Ph.D.
Director
Division of Chemistry I
Office of Generic Drugs
Center for Drug Evaluation and Research